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Correlation between leukocyte count and hemoglobin with the incidence of febrile seizures at RSUD Abdul Wahab Sjahranie Samarinda



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ABSTRACT

Background: Febrile seizures occur at the age of 6 months to 5 years, ranging from 2-5% of cases in children. The sign when the body is fighting infection is the process that occurs, the presence of infection in the body causes a change in the leukocyte count, and high fever can trigger a decrease in hemoglobin. This study aims to determine the relationship between leukocytes and hemoglobin with the incidence of febrile seizures in children.

Methods: This research is analytic observational with a cross-sectional design. The research data was taken from medical records at Abdul Wahab Sjahranie Hospital Samarinda with a purposive sampling method. The study sample was children aged 6 months to 5 years who had febrile seizures and fever without seizures and met the inclusion and exclusion criteria. Statistical analysis of this study used the chi-square test.

Results: The chi-square test results were obtained on hemoglobin and leukocyte count with the incidence of febrile seizures with a p-value on the number of leukocytes ($p=0.032$) and hemoglobin ($p=0.019$).

Conclusion: There is a significant relationship between the number of leukocytes and hemoglobin with the incidence of febrile seizures in children.

Keywords: Febrile Seizure, hemoglobin, leukocyte count.

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INTRODUCTION

Febrile seizures are the most common neurological disorders in children. Febrile seizures are seizures in children aged 6 months to 5 years who experience increased body temperature (temperature above 38°C) caused by processes originating from the extracranial.¹ Most febrile seizures are often found at the age of 1 to less than 2 years. Besides, boy has more febrile seizures (66%) than girls (34%), and the peak age incidence of febrile seizures occurs at 18 months of age.^{2,3} Pediatric febrile seizures in the United States and Western Europe have a 2-5% incidence, with a peak incidence between 12 and 18 months. Meanwhile, the population of pediatric febrile seizures in Asia, namely children in India, experienced 5-10%, and in Japan, 6-9% cases of febrile seizures in children. The highest febrile seizures have ever been reported in Guam, with an incidence of up to 14%.⁴ In Indonesia, the number of cases of pediatric febrile

seizures recorded in 2012-2013 ranged from 3-4%.⁵ Research data that has been carried out at Abdul Wahab Sjahranie Hospital Samarinda from 2016 to 2017 using the case-control method obtained a total of 62 patients with details there were 31 cases of children with febrile seizures and 31 cases of children with fever without seizures due to ARI.⁶

The etiology of febrile seizures is not known with certainty; there appear to be several important factors that cause the development of seizures. Risk factors that can cause febrile seizures in children include age, family history, prenatal history (an age when the mother is pregnant), and perinatal history (asphyxia and low birth weight). The temperature has a risk factor for seizures in children, with a threshold value ranging from 38.3 to 41.4. These threshold signs indicate a risk of a very high temperature or a temperature that is not too high in children, causing seizures.⁷ Other risk

factors that can cause febrile seizures are exposures in the mother's womb, such as mothers who consume cigarettes and the stress of pregnant women.⁸ Fever is often caused by acute respiratory infections, otitis media, pneumonia, gastroenteritis, and urinary tract infections.⁹

Leukocytes are a unit of the body's defense system. The bone marrow forms leukocytes themselves, and some are formed in the lymph tissue. Then after being formed, these leukocytes will be distributed and transported to the circulatory system to other parts of the body, especially leukocyte cells will go to areas experiencing an infection.¹⁰ Cases of fever characterized by infection can manifest seizures. The process of fever will increase basal metabolism and increase oxygen demand, this can result in disruption of hemostasis in neuron cell membranes so that sodium ions that are normally outside the cell enter the cell so that cell depolarization occurs and causes

the release of electrical charges in cells in the brain that lead to seizures.¹¹

One of the markers of the body experiencing infection is an increased number of leukocytes. The increase in leukocyte cells is a sign of the production of cells to fight the presence of foreign antigens or microorganisms that enter the body. When the body is infected with an infection, leukocytes will carry out the process of destroying these microorganisms.¹¹

Hemoglobin is a protein complex consisting of 2 groups, namely heme and globin, in a state of Hb below normal it is called anemia.¹² The role of hemoglobin is to help red blood cells bind oxygen that the body needs to produce energy.¹³ Hb below normal can interfere with the process of decreasing oxygen transport to tissues, causing tissue hypoxia and decreasing metabolic processes of brain development and activity.¹⁴

In the case of low Hb, there will be disruption of ATP, the ATP functions in the active transport activity of sodium and potassium. Active transport of these ions can disrupt the hemostasis of ions inside and outside the cell, thereby disrupting the intracellular and extracellular sodium ion concentrations. Changes in the cell membrane potential of these neurons can make the cell membrane in a state of depolarization and cause the release of electrical charges that lead to seizures in children.¹¹ The state of anemia caused by iron deficiency will interfere with the functions of the central nervous system. Changes strongly influence brain growth in iron status because iron plays a role in the myelination process, metabolism, and the process of neurotransmitters. The excitatory neurotransmitter that plays a role is glutamic acid and the inhibitory one is gamma-aminobutyric acid (GABA) which plays a role in the occurrence of seizures in children.¹³

Based on this, it can be concluded that the leukocyte count and hemoglobin have the potential to be predictors of the incidence of febrile seizures in children. Therefore, an analytical study is needed regarding the correlation between leukocyte count and hemoglobin with the degree of dengue infection in children at Abdul Wahab Sjahranie Hospital, Samarinda.

METHODS

This study is an analytical observational study using a cross-sectional design that aims to determine the relationship between the number of leukocytes and hemoglobin with febrile seizures in children at Abdul Wahab Sjahranie Hospital, Samarinda. This study consisted of 2 variables, the independent variable was leukocyte and hemoglobin levels and the dependent variable was fever. The sampling method was carried out using the purposive sampling method. This research data was taken from medical records at Abdul Wahab Sjahranie Hospital Samarinda in February 2022.

The inclusion criteria were: 1) Patients with complete medical record data and according to the needs of the study, namely leukocyte count and hemoglobin. 2) Patients who have been diagnosed with febrile seizures and fever without seizures who have been hospitalized after the end of treatment until they are cured are determined by a Pediatrician. Exclusion criteria were: 1) Pediatric patients caused by intracranial infection. 2) Pediatric patients with growth and development disorders (microcephaly, cerebral palsy, motoric delayed, speech delayed). 3) Pediatric patients with neurological disorders before the seizure. 4) Pediatric patients with other comorbidities during treatment (malignancy, brain trauma,

congenital disease). The flow of this study was preceded by sampling carried out by purposive sampling technique, namely by taking patient medical record data with inclusion and exclusion criteria. Furthermore, patients who meet the criteria are consulted with a Pediatrician to determine which patients are eligible to be used as samples.

The total samples were 182 samples consisting of 92 febrile seizures and fever without seizures. Bivariate analysis using Chi-square statistical test. The results are significant if $p < 0.05$ with all data analyzed using SPSS 26.0 software.

RESULTS

The total number of samples in the study was 184 samples involved in this study, consisting of 92 febrile seizure patients and 92 febrile patients without seizures. The characteristics of the study subjects are listed in **Table 1**. showing the gender of the cases of febrile seizures in 63 male (68.5%) and 29 (31.5%) patients. The most febrile seizure patients were aged 13-24 months, 39 patients, followed by 6-12 months, 25-36 months, 48-60 months, and 37-48 months.

Table 2 shows the bivariate analysis using the chi-square test. There was a relationship between the number of leukocytes and the incidence of febrile seizures in children with a p-value = 0.032

Table 1. Characteristic of Respondent

Characteristic	Febrile Seizure		Fever without Seizure		Total Sample n (%)
	Total (n)	Percentage (%)	Total (n)	Percentage (%)	
Age range (Month)					
6-12	21	22.8	29	31.5	50 (27.2)
13-24	39	42.4	20	21.7	59 (32.1)
25-36	17	18.5	8	8.7	25 (13.6)
37-48	12	13	16	17.4	28 (15.2)
49-60	3	3.3	19	20.7	22 (12.0)
Gender					
Male	63	68.5	49	53.3	112 (60.9)
Female	29	31.5	43	46.7	72 (39.1)
Leukocyte count					
Leukocytosis	36	39.1	20	21.7	56 (30.4)
Normal	48	52.2	59	64.1	107 (58.2)
Leukopenia	8	8.7	13	14.1	21 (11.4)
Hemoglobin					
Normal	66	71.7	79	85.9	145 (78.8)
Anemia	26	28.3	13	14.1	39 (21.2)

Table 2. Analysis of correlation between leukocytes count and hemoglobin

Variable	Febrile Seizure		Fever without Seizure		P-value
	Total (n)	Percentage (%)	Total (n)	Percentage (%)	
Leukocyte count					
Leukocytosis	36	39.1	20	21.7	0.032
Normal	48	52.2	59	64.1	
Leukopenia	8	8.7	13	14.1	
Hemoglobin					
Normal	66	71.7	79	85.9	0.019
Anemia	26	28.3	13	14.1	

($p < 0.05$) and there was a relationship between hemoglobin and the incidence of febrile seizures with a p -value = 0.019 ($p < 0.05$).

DISCUSSION

Febrile seizures are clinical manifestations due to excessive electrical discharge in brain neuron cells due to intracellular and extracellular electrical control disturbances.¹⁵ Fever is a major factor in febrile seizures. Studies conducted by Gourabi said viral infections of the upper respiratory tract and digestive tract were the most common cause of febrile seizures at the age of 6 months to 5 years.¹⁶

The age of patients who experienced the most febrile seizures was children aged 13-24 months as many as 39 patients (42.4%), followed by those aged 6-12 months as many as 21 patients (22.8%). This is in line with research conducted in Batu city in 2020, the most common group was at the age of 13-24 months as many as 19 patients (46.3%).¹⁷ Children aged 6 months to 3 years are most susceptible to febrile seizures with a peak incidence at 18 months of age.¹⁸ This is related to the phase of brain development, namely the developmental window that easily triggers febrile seizures in children.¹³ The developmental window period is a period of excitability that is more dominant than the inhibitory system, if a child experiences stimulation such as fever during the excitability brain phase, seizures will easily occur when compared to a mature brain.¹⁹

Characteristics based on gender in this study, most samples were found in the male sex who experienced febrile seizures in children. In terms of growth and development, boys tend to be slower than girls, slightly faster.²⁰ This is related

to the ability of cerebral cell maturation in girls which is faster than in boys.²¹ In infancy, the severity of infectious diseases is more common in boys because there are differences in the body's humoral and cellular immune responses in women. In essence, boys have testosterone, this hormone has an effect that can suppress the immune response because it can reduce the secretion of IFN-Gamma and IL-4 by T lymphocyte cells.²² When a person has an infection, a fever can occur, increasing the basal metabolism and oxygen demand. This can lead to a change in the permeability of the neuron cell membrane and the depolarization of the neuron cell which causes seizures in a child.¹⁵

Leukocytes are a unit of the body's defense system, leukocytes are formed by bone marrow and some are formed in lymph tissue which then after being formed will be distributed and transported into the circulatory system to other areas of the body, especially leukocytes will go to areas that are infected or there are microorganisms.¹⁰ The results showed a relationship between the number of leukocytes and the incidence of febrile seizures in children with $p = 0.032$ ($p < 0.05$). This study is in line with research conducted by Biyani et al in the period September 2015 to 2016 and research conducted by Rasyid et al in Pekanbaru in 2019. There is a relationship between the number of leukocytes the incidence of febrile seizures in children.^{11,23} Decreased leukocytes can occur due to viral infections such as influenza, hepatitis, and measles. Microbes originating from outside the body are exogenous pyrogens that stimulate macrophage cells, leukocytes, and other cells to form endogenous

pyrogens, resulting in fever. Factors that cause high leukocytes include bacterial and fungal infections, and inflammation (inflammation).²⁴

A febrile seizure is a disease caused by clinical manifestations of fever, in someone who has a fever is usually caused by infection. One of the signs of infection in a person is a high number of leukocytes, the number is influenced by an increase in the production of cells to fight an infection that occurs. When infection occurs, leukocytes will automatically carry out the phagocytosis process or destroy microorganisms that cause infection.¹¹ The body's immune system contains cells that play a role in the body's natural immune system such as phagocytic cells which will later envelop and destroy microorganisms or foreign antigens that enter the body.²⁵ With the manifestation of fever, an increase in body temperature of 10C will increase the basal metabolism by 10-15% and an increase in oxygen demand of 20%, causing changes in neuron cell membranes. This affects sodium ions which are generally many outside the cell to enter the cell, resulting in depolarization of the cell and an electrical discharge in the brain resulting in seizures in children.¹¹

Hemoglobin level is one indicator to determine the occurrence of anemia, iron deficiency anemia is the most common anemia found in Indonesia. The 2001 Household Health Survey (SKRT) results showed that the prevalence of iron deficiency anemia in Indonesia in children under five was 55.5%.²⁶ The results showed a relationship between hemoglobin and the incidence of febrile seizures with a p -value = 0.019 ($p < 0.05$). This is in line with research conducted by Dasmayanti in Banda Aceh in 2013 and Anidar *et al* in Aceh in 2020 which showed a significant relationship between hemoglobin and the incidence of febrile seizures in children.^{13,27}

Iron deficiency anemia is closely related to febrile seizures in toddlers due to unstable intake and high demand. Lack of hemoglobin in the blood can cause red blood cells to decrease binding oxygen. In contrast, oxygen plays a role in metabolic processes, including the development and activity of cells in the brain. If the anemia is caused by iron deficiency, the iron content in the brain is reduced.²⁸ Iron deficiency

anemia can induce seizures in a child through the mechanism of hypoxemia, changes in brain nerve metabolism, and myelination disorders. Iron also plays a role in the activity of aldehyde and monoamine oxidase enzymes, which are very important in the normal rate of degradation of neurotransmitters.²⁹ Iron deficiency anemia also affects neurotransmitter systems such as norepinephrine, dopamine, serotonin, gamma-aminobutyric acid (GABA), and glutamic acid.³⁰ Imbalances between excitatory and inhibitory neurotransmitters can cause seizures in children.²⁶ Children who have anemia are closely related to the ability of red blood cells to bind oxygen. This oxygen plays a role in the active transport of Na-K ions in stabilizing nerve membranes. If this is disturbed, it can interfere with the concentration of sodium ions in the cell, resulting in a change in nerve cell permeability and causing excessive depolarization which causes seizures.¹³

This research has several limitations: 1) Data collection on the child's birth weight is only taken through medical records, which are only memories from the patient's parents, not from direct recording at the time the baby is born. 2) Most medical record sheets do not include data on the child's height, so it is quite difficult to assess a child's nutritional status based on weight/TB if only using the patient's medical record. 3) The measurement of the child's temperature is the temperature at the time of admission to the hospital, so it is impossible to know the temperature at the time of the seizure.

CONCLUSION

The incidence of cases with febrile seizures were males who had a greater incidence of febrile seizures and were in children aged 13-24 months. There is a significant relationship between the leukocyte count and hemoglobin with the incidence of febrile seizures in children.

ETHICAL CLEARANCE

This research has passed the ethical feasibility test by the health research ethics committee of RSUD Abdul Wahab Sjahranie Samarinda

CONFLICT OF INTEREST

The author declares that there is no conflict of interest in the publication of this article

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AUTHOR CONTRIBUTIONS

All authors were involved in contributing to all processes in this research, in the form of concept, design, and monitoring as well as data collection and analysis, preparation, and approval for publication of this manuscript.

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